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| ART UNIT | PAPER NUMBER |
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| 1656 | |

DATE MAILED: 09/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/699,394 | DRABORG ET AL. | |
| | Examiner | Art Unit | |
| | William W. Moore | 1656 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *05 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *10-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.



SDV

## DETAILED ACTION

### *Restriction*

Restriction to one of the following inventions is required under 35 U.S.C. § 121:

I. Claims 1-9 drawn to several hundred species of modified proteases comprising single and multiple amino acid sequence modifications at diverse positions registered by correspondence with the amino acid sequence of the mature subtilisin BPN' and compositions comprising same, classified in class 435, subclass 221.

II. Claims 10-15 drawn to several hundred species of DNA sequences encoding modified proteases comprising single and multiple amino acid sequence modifications at diverse positions registered by correspondence with the mature subtilisin BPN' amino acid sequence, vectors and host cells comprising same, and methods of using same in a recombinant method of making the protease, classified, *inter alia*, in class 536, subclass 23.2.

The inventions are distinct, each from the other because of the following reasons:

Inventions of Groups I and II are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the product as claimed can be made by another and materially different process such as solid-phase chemical synthesis.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

This application contains claims directed to the following patentably distinct species of the claimed invention:

Group I, claims 1-9, is generic to a plurality of disclosed patentably distinct protease species comprising over $2 \times 10^{13}$ multiple modifications indicated in clause (a) of claim 1 alone, which includes the 628 individual and multiple modification sets stated in claim 3. Applicant is required under 35 U.S.C. § 121 to elect a single disclosed species, even though this requirement is traversed.

Group II, claims 10-15, is generic to a plurality of disclosed patentably distinct DNA sequence species encoding the over $2 \times 10^{13}$ multiple modifications indicated in clause (a) of claim 1 alone, which includes the 628 individual and multiple

modification sets stated in claim 3. Applicant is required under 35 U.S.C. § 121 to elect a single disclosed species, even though this requirement is traversed.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. § 103(a) of the other invention.

*Election*

During a telephone conversation with Mr. Elias Lambiris on 16 September 2005 a provisional election was made **with** traverse to prosecute the invention of Group I, wherein the protease variant species further elected has at least one of an insertion, substitution, or deletion of one among twenty different amino acids at position 62, which according to page 23 of the specification, may be the subtilisin BPN'-correspondent position 62 set forth in SEQ ID NO:1, together with any one of the further modifications recited at lines 6-27 of claim 1, which are also present, in part, in claims 2 and 6. Accordingly, claims 1-9 are examined herein to the extent that they describe a modification at the subtilisin BPN'-correspondent position 62 combined with either of the N76D, S substitutions. Claims 10-15 are withdrawn from consideration as drawn to an unelected invention. Affirmation of this election must be made by applicant in replying to this Office action.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee withdrawn required under 37 CFR 1.17(i).

*Priority*

Applicant's claims at the first page of the specification filed 31 October 2003 to priority under U.S.C. § 119 of the 8 November and 18 December 2002 filing dates of the Danish patent applications Nos. 2002 01705 and 2002 01933, as well as Applicant's

claims to domestic priority of the 18 November and 19 December 2002, as well as the 1 October 2003, filing dates of US provisional applications Nos. 60/427,156, 60/434,723, and 60/507,537, is hereby acknowledged.

*Specification*

Compliance with 37 CFR § 1.821 is required in response to this Office action. The specification is objected to because claims 1, 2, and 4-9 do not have designations that describe their subject matters according to the requirements of 37 CFR § 1.821 for a Sequence Disclosure. Even if a reference amino acid sequence had been set forth in, e.g., claim 1, a recitation of a nucleotide or amino acid sequence position must also include a statement of the designation, **"SEQ ID NO:n"**, where "n" is an integer corresponding to the Sequence Disclosure. See, e.g. claim 3, not a basis of this objection to the specification where its closing clause (b) recites such a designation. 37 CFR § 1.821 also requires that sequence identifiers accompany descriptions of defined nucleotide and amino acid sequences in the specification, e.g., pages 2 and 3, with a designation properly stated as **"SEQ ID NO:n"**. See 37 CFR §§ 1.821(b), (c) and (d).

*Claim Objections*

Claims 1-3 are objected to because of the following informalities: Although claims 1-3 provide comprehensive descriptions of their intended subject matter, the subject matter is not organized well enough to permit ready comprehension of the intended variations. Appropriate correction is required, such as, e.g., placing the simplest aspect of claim 1 - which is clause (c) - first, then placing the next most complex aspect of the claim - which is clause (b) - second and providing a separate line for each set of modifications, and closing the claim with clause (a), placing each of the 49 positions for secondary modification on a separate line of the claim, as well as prefacing the subject matters of clauses (b) and (c) with a transitional phrase indicating - if this is indeed

Applicant's intent - that amino acid sequence modifications are required in at least two amino acid positions. Similarly, providing a separate line for modifications, in numerical order of the first position to be modified, in claim 2 is required. Likewise, providing a separate line for modifications, in numerical order of the first position to be modified, for the 680 species of modifications in claim 2 is required.

*Claim Rejections - 35 USC § 101*

35 U.S.C. § 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-7 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1-7 do not describe a "new . . . composition of matter" as required by the statute because they fail to distinguish a "variant" protease that is present in Nature in its native state from a "variant" protease that is a discovery, an invention reduced to practice by the efforts of a person. This rejection may be overcome by amending each independent claim to introduce an appropriate distinguishing term such as, e.g., reciting "[a]n **isolated** . . . protease" or "[a] modified protease".

*Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, and 4-9 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification fails to exemplify or describe the preparation of the divergent molecules of claims 1, 2, and 4-7 that function have more than ten amino acid sequence

modifications relative to the amino acid sequence of subtilisins BPN' or 309, discussed in the specification, or the compositions of claims 8 and 9 comprising them, where the molecule that is modified is other than a microbial subtilase such as those discussed at, e.g., page 1, lines 12-14, and page 2, line 5, of the specification. Only claim 3 recites a particular reference sequence amino acid sequence that, prior to modification, permits an identification of the positions for modification according to the disclosed invention, positions that are applicable only to the structures of microbial subtilases. Furthermore, the specification discloses no concurrent modification of more than ten amino acid positions in a subtilase, see the bottom of the left column at page 11. Thus the claims are rejected because they reach generic proteases that differ at multiple amino acid sequence positions after alteration, subject matter not disclosed in the specification, and also because they reach subtilases sustaining at more than 10 positions in a subtilase, indeed at as many as 149 positions according to claim 1, which extent of modification is not disclosed in the specification.

In addition, the specification fails to exemplify or describe the preparation of the subject matters of the divergent molecules of claims 1, 2, and 4-9 that will not function as proteases, or the compositions of claims 8 and 9 comprising them. Unlike claim 3, not subject to this rejection because it requires a "variant [that] has protease activity", the rejected claims reach molecules that, even though the starting molecule may have been a subtilase, have some activity other than proteolytic activity after modification. "While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of the first paragraph of 35 U.S.C. § 112. *Fiers v. Revel v. Sugano*, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993). The specification furnishes no relevant identifying characteristics of proteases other than subtilases that diverge at

the amino acid positions recited in the claims, because the recited amino acid positions are recognizable only by correspondence to the disclosed reference subtilisin amino acid sequence set forth in SEQ ID NO:1, and have no particular correspondence to a generic protease amino sequence. The specification also fails to furnish any relevant identifying characteristics of subtilases that diverge concurrently at more than ten amino acid positions, or that have an altered function, after modification at the one-hundred and forty-nine positions recited in clause (a) of claim 1. Nothing demonstrates that, at the time the specification was filed, Applicant was "able to envision" enough of the structure of any of the billions of undisclosed, multivariant, proteases – or nonproteases – resulting from all permutations of the combinations available in claim 1 to provide the public with identifying "characteristics [that] sufficiently distinguish [them] . . . from other materials". *Fiers*, 25 USPQ2d at 1604 (citing *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991). The specification's treatment of the claimed subject matter is considered to be entirely prospective where skilled artisans in the relevant field of molecular biology could not predict the structure, or other properties, of the generic proteases of claims 1, 2, and 4-7.

Claims 1, 2, and 4-7 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for the preparation of modified subtilases having no more than ten amino acid sequence modifications at positions selected for modification numbered according the amino acid sequence of the mature subtilisin BPN' set forth in SEQ ID NO:2, does not reasonably provide enablement for the preparation of modified, generic proteases having as many as 149 amino acid sequence modifications at positions recited in the claims if numbered according to no particular subtilase amino acid sequence. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1, 2, and 4-7 contemplate an arbitrary assignment of any or all of amino acid substitutions, additions or deletions at more than 149 separate positions – where some positions may sustain more than a single modification, e.g., both an insertion and a substitution – in any conceivable protease. This rejection is stated under the first

paragraph of the statute because the specification cannot support introduction of more than ten amino acid alterations in the amino acid sequence of a generic protease yet yield a useful product, i.e., a variant subtilase that retains proteolytic activity. Indeed, Applicant's specification can identify positions for non-disruptive modifications recited in the claims only when they are numbered according to the amino acid sequence of the mature, class I-S2 subtilase, subtilisin BPN', particularly where a particular amino acid at a particular position must be substituted by another, and where no more than a few modifications are made concurrently in a subtilase amino acid sequence.

It is well settled that 35 U.S.C. § 112, first paragraph, requires that a disclosure be sufficiently enabling to allow one of skill in the art to practice the invention as claimed without undue experimentation and that unpredictability in an attempt to practice a claimed invention is a significant factor supporting a rejection under 35 U.S.C. §112, first paragraph, for non-enablement. See, *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (discussing eight factors relevant to analysis of enablement). Applying the analytical factors discussed in *Wands* to Applicant's disclosure, it is apparent that:

a) the specification lacks adequate, specific, guidance for altering the amino acid sequences of proteases other than the microbial subtilases to the extent recited in the claims and lacks adequate guidance for making more than ten concurrent modifications in a subtilase amino acid sequence,

b) the specification lacks working examples wherein proteases, even the microbial subtilases, are altered to the extent permitted by, e.g., claim 1,

c) in view of the prior art publications of record herein, the state of the art and level of skill in the art do not support such alteration, and,

d) unpredictability exists in the art where no proteases other than the microbial subtilases have yet had more than a few amino acids specifically identified for concurrent modification and retained proteolytic activity.

Thus the scope of subject matters embraced by terms admitting modification of generic proteases, and permitting more than ten concurrent modifications in a subtilase, is unsupported by the present specification even if combined with teachings available in the prior art made of record herewith.

*Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, from which claims 2-9 depend, recites no sequence identifier for the amino acid sequence of a reference subtilisin with which the recited positions for modification can be identified by correspondence, thus claims 1, 2, and 4-9 fail to particularly point out and distinctly claim Applicant's intended subject matter where they fail to place the positions recited for amino acid sequence modification in the context of any reference amino acid sequence. Claims 2 and 4-9 are subject to this rejection of claim 1 because they fail to otherwise clarify the ambiguity of the claim from which they depend. This rejection may be overcome by amending claim 1 to insert a clause stating the absent sequence identifier, e.g., "wherein said positions correspond to positions in the amino acid sequence of the mature subtilisin BPN' set forth in SEQ ID NO:1". See, e.g., clause (b) of claim 3 not subject to this rejection, however, a recitation of the reference amino acid sequence, and its sequence identifier, should appear in the preamble of each independent claim, rather than at the close of the claim as in claim 3.

Claim 1 is further indefinite in reciting, in clause (b), "one of the following combination variants" because the claim appears to recite, in view of the non-uniform punctuation of clause (b) of the claim, modifications that are not combinations. See, e.g., lines 3, 5, 9-10, 12 and 13 within clause (b) where single modifications at single positions are indicated, set off by commas. Only clause (c) of claim 1 permits single amino acid sequence modifications, and only at position 68. Claim 3 is indefinite in reciting a dependency from claim 1 but stating several single position amino acid sequence modifications among its 680 species that are not modifications at position 86.

Claim 2 is not subject to this rejection because it requires modifications in at least two amino acid positions according to clause (a) of claim 1, but claims 4-9 are subject to this rejection because they depend from claim 1 but fail to resolve the ambiguity of clause (b) thereof. This aspect of the rejection may be overcome by amending claim 3 to make it an independent claim and by removing clause (b) from claim 1 and, where its recited single position modifications are not found among the modifications of claim 3, reciting the additional modifications in a separate, independent claim.

Claim 1 is further indefinite in reciting in clause (a), "in one or more of the positions" and "at least one of the following modifications", because the series of positions that follow these phrases is indefinite in scope because they are not stated in a proper Markush format, where the positions in the first part of the clause, and the modifications in the second part of the clause, are not "selected from the group consisting of" and the final position or modification is not preceded by the conjunction "and". The public and the artisan seeking to determine the metes and bounds of the intended subject matter cannot know whether other or not other positions or modifications are to be included in addition to those recited. See, e.g., clause (c) of claim 1 which is not a basis for this aspect of the rejection. Claims 2-9 are included in this aspect of the rejection because they fail to resolve the ambiguity of clause (a) of claim 1 from which they depend.

Claim 1 is further indefinite in reciting ,"one of the following combination variants", in clause (b) because the scope of the various series of combinations of modifications, or single modifications where no combination actually appears, following this introductory phrase is indefinite because the group of modifications is not stated in a proper Markush format, i.e., combinations are not "selected from the group consisting of" and the final combination is not preceded by the conjunction "and". The public and the artisan seeking to determine the metes and bounds of the intended subject matter cannot know

whether other or not other combinations are to be included in addition to those recited. See, e.g., clause (c) of claim 1 which is not a basis for this aspect of the rejection. Claims 2-9 are included in this aspect of the rejection because they fail to resolve the ambiguity of clause (b) of claim 1 from which they depend.

Claim 3 is independently indefinite in reciting in its preamble, "one or more of the following alteration", because the subsequent series of 680 single and multiple amino acid sequence modifications is indefinite in scope because they are not stated in a proper Markush format, where the modifications are separated by appropriate punctuation, are not "selected from the group consisting of" and the final modification is not preceded by the conjunction "and". The public and the artisan seeking to determine the metes and bounds of the intended subject matter cannot know whether other or not other modifications are to be included in addition to those recited or the modifications might be taken jointly as well as severally.

Claims 4 and 5 are independently indefinite in reciting, "wherein the parent subtilase . . ." because claim 1, from which they depend, provides no antecedent basis for the term "parent".

Claim 7 is indefinite in reciting five modifications among the nine indicated because none of the modifications S101G, S103A, G159D, M322V, and Q236H find an antecedent basis in claim 1 from which claim 7 depends. Amending claim 7 to depend from claim 1 will overcome this aspect of the rejection.

*Double Patenting*

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 and 4 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,245,901. Although the conflicting claims are not identical, they are not patentably distinct from each other because modifications of the subtilase of the patented claim are included in modifications of subtilases of claims 1 and 4 herein.

Claims 1, 5, 8 and 9 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 78 and 122 of the copending, commonly-assigned, Application No. 09/957,806. Although the conflicting claims are not identical, they are not patentably distinct from each other where modifications of subtilases, and compositions comprising same, of claims of the copending application, where a "savinase-like" enzyme is a class I-S2 subtilase, are included in modifications of subtilases, and compositions comprising same, of claims 1, 5, 8 and 9 herein. This is a provisional obviousness-type double patenting rejections because the conflicting claims have not in fact been patented.

*Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1, 4, and 8 are rejected under 35 U.S.C. § 102(b) as being anticipated by von der Osten et al., US 6,245,901, made of record herewith.

Von der Osten et al. are available as prior art in view of their effective US filing date of 15 October 1991 for their disclosure, see claim 1, of the class I-S1 subtilase PD48

having "one or more" amino acid substitutions including S9K and R62K, meeting limitations of clause (a) of claims 1 and 4 herein which permit a lysine substitution at position 62 as well as a substitution S9K, meeting limitations of claims 1 and 4 herein. Von der Osten et al. also disclose, col. 20 at lines 40-56, detergent compositions that comprise the modified subtilase of their claim 1, meeting limitations of claim 8 herein.

Claims 1-9 are rejected under 35 U.S.C. § 102(e) as being anticipated by Poulouse et al., US 6,312,936, US 6,482,628, and US 6,927,055, all made of record herewith.

Poulouse et al. commonly disclose, see line 14 in Table 3 at cols. 27-28 of the '936 patent, a generic subtilase comprising, *inter alia*, the several amino acid substitutions of N62D, S101G, S103A, V104I, G159D, A232V, Q236H, Q245R, N248D, and N252K, meeting limitations of clause (a) of claim 1, as well as the limitations of claims 2-7 herein. Poulouse et al. also disclose a detergent composition comprising the modified subtilase as well as other enzymes, such as other proteases, lipases, amylases, and cellulases at col. 19 lines 32-65, meeting limitations of claims 8 and 9 herein.

Claims 1-9 are rejected under 35 U.S.C. § 102(e) as being anticipated by Ghosh et al., US 6,376,450, US 6,610,642, and US 6,838,425, all made of record herewith.

Ghosh et al. commonly disclose, see line 5 in Table 3 at cols. 25-26 of the '450 patent, a generic subtilase comprising, *inter alia*, the several amino acid substitutions of N62D, S101G, S103A, V104I, G159D, A232V, Q236H, Q245R, N248D, and N252K, meeting limitations of clause (a) of claim 1, as well as the limitations of claims 2-7 herein. Ghosh et al. also disclose a detergent composition comprising the modified subtilase as well as other enzymes, such as other proteases, lipases, amylases, and cellulases at cols. 67-78, meeting limitations of claims 8 and 9 herein.

Claims 1-4, 6, 8 and 9 are rejected under 35 U.S.C. § 102(e) as being anticipated by Brode et al. et al., US 6,436,690, US 6,455,295, and US 6,475,765, all made of record herewith.

Brode et al. commonly disclose, see cols. 4-7 and Tables 3-5 and 22-25, in, e.g., the '690 patent, modified class I-S1 subtilases subtilisin BPN', subtilisin Carlsberg, and subtilisin DY comprising combinations of the substitution N62D with one or more of the substitutions V95T; G97E,D,N; A98,S,D,E,T,Q,N; S99D; G100S; and A215D, meeting limitations of clause (a) of claim 1, as well as limitations of claims 2-4 and 6 herein. Brode et al. also disclose detergent compositions, see, e.g., cols 53-63 of the '690 patent, comprising the modified subtilase and other enzymes, such as other proteases, lipases, amylases, and cellulases, meeting limitations of claims 8 and 9 herein.

Claims 1-3, 5, 6, 8 and 9 are rejected under 35 U.S.C. § 102(e) as being anticipated by Brode et al. et al., US 6,599,730, made of record herewith.

Brode et al. disclose, see cols. 5-7 and Tables 4-5 and 33-37, modified class I-S2 subtilisins 309 comprising combinations of the substitution N62D, which is N60D in the subtilisin 309 amino acid sequence, with one or more subtilisin BPN'-correspondent substitutions of V95T; G97E,D,N; A98,S,D,E,T,Q,N; S99D; G100S; and A215D, meeting limitations of clause (a) of claim 1, as well as limitations of claims 2, 3, 5 and 6 herein. Brode et al. also disclose a detergent composition comprising the modified subtilase as well as other enzymes, such as other proteases, lipases, amylases, and cellulases at cols. 96-108, meeting limitations of claims 8 and 9 herein.

Claims 1, 5 and 9 are rejected under 35 U.S.C. § 102(e) as being anticipated by Roggen et al., US 2005/0181446, made of record herewith.

Roggen et al. are available as prior art in view of their effective US filing date of 21 September 2001 for their disclosure, see claim 78, of a "savinase-like subtilase having "one or more" amino acid substitutions including S9K and R62K, meeting limitations of clause (a) of claim 1, as well as claim 5 herein, which permits a substitution of lysine at a position in any protease 62 as well as a substitution S9K in any protease. Roggen et al. also disclose a detergent composition comprising the modified subtilase in claim 122.

*Conclusion*

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 571.272.0933 and whose FAX number is 571.273.0933. The examiner can normally be reached Monday through Friday between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Primary Examiner, Dr. Kathleen Kerr, can be reached at 571.272.0931. The official FAX number for all communications for the organization where this application or proceeding is assigned is 571.273.8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571.272.1600.

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20 September 2005

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